Remarks

Introduction

Claims 23-25 and 42-50 were pending. By way of this response, claim 23 has been amended, and claims 45-50 have been cancelled without prejudice. Support for the amendments to the claims can be found in the specification as filed, and care has been taken to avoid adding new matter. Accordingly, claims 23-25 and 42-44 are currently pending.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 23-25 and 42-44 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.

Claim 23 has been amended to make more clear that different antibodies are used to specifically bind hyperglycosylated human chorionic gonadotropin (hHCG) and human chorionic gonadotropin (HCG), and to antecedence of the term "standards".

In view of the above, applicant submits that the rejections under 35 U.S.C. § 112, second paragraph have been overcome, and applicant respectfully requests withdrawal of the rejection.

Rejections Under 35 U.S.C. § 103

Claims 23-25, 42, and 43 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over O'Connor et al. (U.S. 6,500,627; hereinafter O'Connor) in light of Birken et al. (2001; hereinafter Birken 2001) in view of Hochstrasser et al. (US 2003/0157580; hereinafter Hochstrasser) and Birken et al. (US 6,521,416; hereinafter Birken '416). Claim 44 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over O'Connor in light of Birken 2001 in view of Hochstrasser and Birken '416, and further in view of Campbell et al. (US 4,946,958; hereinafter Campbell).

Applicant traverses the rejections of the present claims.

The primary reference, O'Connor, discloses the use of antibodies that bind to an early pregnancy associated molecular isoform of HCG and non-nicked HCG to predict pregnancy outcome, for detecting non-trophoblast malignancy, and for detecting gestational trophoblast disease (e.g., see column 6, lines 6-26; column 8, line 62-column 9, line 17; and column 9, lines 35-62). Importantly, O'Connor only discloses methods of detecting a trophoblast disease in pregnant women (i.e., gestational trophoblast disease). Furthermore, O'Connor discloses that the methods of detecting gestational trophoblast disease are based on comparing the ratio of the early pregnancy associated molecular isoform of hCG to the late pregnancy associated molecular isoform of hCG over time, wherein a continuing high ratio indicates the presence of gestational trophoblast disease (column 9, lines 52-62).

The first secondary reference, Hochstrasser, discloses an assay for heart fatty acid binding protein (H-FABP) and brain fatty acid binding protein (B-FABP) to detect transmissible spongiform encephalopathies (TSEs), such as Creutzfeldt-Jakob disease (CJD). Hochstrasser discloses using two assays used to detect CJD, one which determines the concentration of H-FABP in a sample, and one which is specific for an acute myocardial infarction (AMI), which is also typically associated with the presence of H-FABP. If the first assay is positive for H-FABP, and the second assay is negative for AMI, the patient being tested may be suffering from CJD (e.g., see paragraph [0012]).

The other secondary reference, Birken '416, discloses methods for predicting the likely timing of the onset of menopause for a perimenopausal female by determining the amount of human luteinizing hormone beta core fragment (hLHβcf) in a sample, and a method for assessing ovarian function and determining the efficacy of hormone replacement therapy in a perimenopausal woman using anti-hLHβcf antibodies (e.g., see column 4, lines 17-39; and column 5, lines 16-63).

The tertiary reference, Campbell, discloses various chemiluminescent acridinium compounds used as labels in immunoassays.

Applicant submits that the references, taken alone or in any combination, do not disclose or suggest the present invention. For example, the references taken alone or in any combination, including the combination of O'Connor, Hochstrasser, and Birken '416, do not disclose or even suggest a method of detecting a trophoblastic disease in a subject that comprises a step of confirming that the subject is not pregnant, as recited in claim 23.

As discussed above, the primary reference, O'Connor, only discloses methods of detecting gestational trophoblastic diseases. In other words, O'Connor only discloses methods of detecting trophoblastic diseases in pregnant women. Thus, O'Connor does not disclose or even suggest a method that comprises a step of confirming that a subject is not pregnant since the diseases being detected by O'Connor are diseases of pregnant women. Applicant submits that O'Connor actually **teaches away** from the presently claimed methods since O'Connor requires the women be pregnant in order to detect the gestational trophoblastic diseases.

Hochstrasser fails to provide the deficiencies apparent in O'Connor. As discussed above, Hochstrasser discloses methods of detecting TSEs using H-FABP and B-FABP. Hochstrasser does not disclose or even suggest a method which includes a step of confirming a subject is not pregnant. Thus, the combination of O'Connor and Hochstrasser fails to disclose or even suggest all of the elements recited in the present claims.

Similarly, Birken '416 fails to provide the deficiencies apparent in O'Connor and Hochstrasser. As discussed above, Birken '416 discloses methods for predicting timing of menopause onset in perimenopausal women. Furthermore, Birken '416 discloses methods which comprise detecting a completely different and distinct antigen (i.e., hHLβcf) than those recited in the present claims. Thus, the combination of O'Connor, Hochstrasser, and Birken '416 fails to disclose or even suggest all of the elements recited in the present claims.

In addition, applicant submits that a person of ordinary skill in the art would not be motivated to combine the deficient teachings of O'Connor, Hochstrasser, and Birken, let alone, to do so and obtain the presently claimed invention. Applicant submits that the methods and assays disclosed by each of O'Connor, Hochstrasser, and Birken, are so different and distinct that a person of ordinary skill in the art would not be motivated to even consider the deficient teachings of either or both of Hochstrasser and Birken in attempting to resolve the deficiencies apparent in O'Connor.

Even if the references could be erroneously combined, the combination would result in the use of antibodies that detect different and distinct antigens from those disclosed by O'Connor, and by those recited in the present claims. It is well established that a reference must be interpreted as a whole, and cannot be picked apart to deprecate an invention (*In re Fine*, 837 F.2d 1071, 1075, (Fed. Cir. 1988)). The rejection in the Office Action appears to be picking and choosing specific portions of both Hochstrasser and Birken '416 without consideration for the teachings of the references in their entireties.

In addition, "as a general rule, references that teach away cannot serve to create a prima facie case of obviousness." (*McGinley v. Franklin Sports, Inc.* CAFC 8/21/01 citing *In re Gurley*, 31 USPQ2d 1131, (Fed. Cir. 1994)). Since the primary reference, O'Connor, actually **teaches away** from the presently claimed methods, applicant submits that O'Connor cannot properly be used to support the rejection of the claims under 35 U.S.C. § 103.

Furthermore, applicant submits that the references taken alone or in any combination do not disclose any method which comprises comparing a determined amount of hyperglycosylated HCG or HCG present in a sample to a 50th percentile of amounts of hyperglycosylated HCG or HCG present in samples obtained from subjects who do not have a trophoblastic disease, respectively, as recited in the present claims.

Applicant submits that the statement in the Office Action that the 50th percentile can be determined by routine experimentation makes obvious the present claims is improper and

incorrect. To properly support a rejection under 35 U.S.C. § 103, the question should be whether the references disclose or specifically suggest steps of comparing the determined amounts of hyperglycosylated HCG or HCG in a sample to a 50th percentile of amounts of hyperglycosylated HCG or HCG in samples obtained from subjects who do not have a trophoblastic disease, respectively.

The Office Action fails to identify any portion of the cited references, or any other prior art document, that discloses or specifically suggests such a method, let alone, the methods recited in the present claims. Any motivation or suggestion to support a rejection under 35 U.S.C. § 103 must be clear and particular (*In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999); emphasis added), and "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed" (*In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000)). Generalized claims of what a person of ordinary skill in the art would have been "well aware" or can determine fail to satisfy the level of specificity that is required to properly maintain a rejection under 35 U.S.C. § 103. The Examiner must point to some concrete evidence in the record in support of factual findings of obviousness, rather than relying on an assessment of what is "well recognized" or what a skilled artisan would be "well aware". *In re Zurko*, 258 F.3d 1379, 1385-86 (Fed. Cir. 2001).

Furthermore, the [obviousness] test requires that the nature of the problem to be solved be such that it would have led a person of ordinary skill in the art to combine the prior art teachings in the particular manner claimed. See In re Rouffet, 149 F.3d 1350, 1357 (Fed. Cir. 1998). "Could have" is analogous to obvious to try. See, e.g., In re Deuel, 51 F.3d 1552, 1559 (Fed. Cir. 1995) ("'Obvious to try' has long been held not to constitute obviousness."). The Office Action states that "the optimum threshold in this case 50th percentile can be determined by routine experimentation ..." (emphasis added). This reasoning is analogous to an "obvious to try" position, which cannot properly serve as a basis to support a rejection under 35 U.S.C. § 103.

Applicant submits that the numerical values recited in the present claims are more than just an optimum threshold, as stated in the Office Action, and that nevertheless, the cited references do not provide any disclosure or suggestion that would have led a person of ordinary skill in the art to combine the teachings of the references in the particular manner being presently claimed.

Thus, applicant submits that O'Connor, Hochstrasser, and Birken '416, taken alone or in any combination, do not disclose or even suggest all of the elements recited in the present claims, and further that a person of ordinary skill in the art would not be motivated to combine the deficient teachings of the references and obtain the presently claimed methods. In view of the above, applicant submits that the present claims, and claims 23-25, 42, and 43 in particular, are unobvious from and patentable over O'Connor, Hochstrasser, and Birken '416, taken alone or in any combination, under 35 U.S.C. § 103.

Regarding claim 44, applicant submits that Campbell fails to provide the deficiencies apparent in O'Connor, Hochstrasser, Birken '416, taken alone or in any combination. For example, Campbell fails to disclose any method which comprises a step of confirming a subject is not pregnant. Thus, at least for the reasons discussed above, applicant submits that the present claims, and claim 44 in particular, is unobvious from and patentable over O'Connor, Hochstrasser, Birken '416, and Campbell, taken alone or in any combination, under 35 U.S.C. § 103.

Conclusion

In conclusion, applicant submits that each of the outstanding rejections have been overcome, and that the present claims are in condition for allowance, notice of which is respectfully requested. If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicant's undersigned representative invites the Examiner to telephone him at the number provided below.

Respectfully submitted,

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/Greg S. Hollrigel, Reg. # 45374/

Greg S. Hollrigel
Registration No. 45,374
Stout, Uxa, Buyan & Mullins, LLP
4 Venture, Suite 300
Irvine, California 92618
Telephone: 949-450-1750